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assessed by analysis of blood samples from 47 workers occupationally exposed to styrene and 47 unexposed controls using the glycophorin A (GPA) *in vivo* genotoxicity assay. This assay utilizes monoclonal antibodies and flow cytometry to analyze erythrocytes from heterozygous GPA(M/N) individuals to enumerate the frequency of variant red cells that have lost expression of a single GPA allele. Two classes of allele-loss variants are detected; hemizygous cells that express the remaining GPA allele at a normal single-copy level (N/Ø cells), and homozygous cells that express the remaining allele at a two-copy level (N/N cells). Any effect of styrene exposure appears to be small and is obscured by confounding effects of the subjects' smoking habits. In exposed workers variant frequencies per million cells (Vfs) were N/Ø = 10.0 ± 9.1 (mean ± 1 SD) and N/N = 7.8 ± 5.7 versus N/Ø = 11.3 ± 9.6 and N/N = 6.9 ± 6.4 in the controls. Further, in the subset of 35 laminators exposed to the highest air concentrations of styrene, no elevation in GPA Vfs was observed: N/Ø = 9.7 ± 7.3, N/N = 8.1 ± 6.2. People who smoked appeared to show increased Vfs independent of styrene exposure. With control and styrene-exposed groups combined, N/Ø Vfs were significantly elevated in smokers, 11.9 ± 10.2 compared to non-smokers, 8.2 ± 5.5 ($p = 0.034$) and N/N Vfs were elevated but not significantly. Excluding smokers from the styrene analysis revealed a trend (not statistically significant) to higher N/Ø and N/N Vfs in the styrene-exposed workers. In 19 exposed workers N/Ø and N/N Vfs were 9.3 ± 6.6 and 7.1 ± 4.7 compared to 6.8 ± 3.3 and 5.2 ± 3.0 respectively in 14 controls. Thus, the data for non-smokers suggest a somatic genotoxic effect of styrene exposure.
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ACRYLAMIDE INDUCED DOMINANT LETHALITY IN MICE FOLLOWING LOW DOSE CHRONIC ADMINISTRATION IN DRINKING WATER. J.B.Bishop[1], R.E.Chapin[1], P.Fail[2], J.D.George[2], T.Grizzle[2], B.M.Sadler[1], J.J.Heindel[1], [1]NIEHS, RTP, NC, [2]Res. Triangle Inst., RTP, NC

Acrylamide, a vinyl monomer, has been shown to induce dominant lethals and heritable translocations in the germ cells of male mice after i.p. injections or dermal applications, and dominant lethals in the germ cells of male rats following oral administration in drinking water. The present test was designed to characterize induction of dominant lethal mutations in the germ cells of mice exposed to chronic, low-levels of acrylamide in drinking water. This test was conducted in conjunction with an NTP Reproductive Assessment by Continuous Breeding (RACB) study in which male and female CD1 mice were dosed continuously for 140 days with 0, 10, 20 or 30 ppm acrylamide in their drinking water. Exposures were estimated to be 0, 1.7, 3.1 or 5 mg/kg/day, respectively. After 20 weeks on study, each of 20 CD1 males per treatment group was caged with 3 untreated, nulliparous CD1 females on each of 4 consecutive nights. Females were killed 16 days following observation of a mating plug (or from the second mating opportunity if no plug was observed) and their uterine contents analysed for the total numbers of implantations and of living fetuses, and for percentages of implants presenting as resorption males and as dead embryos. The percentage of resorptions in the 30 ppm treatment group (12.7%[illegible] was significantly greater than in the control group (4.8%[illegible]). These results are similar to those seen following chronic administration of acrylamide to rats (Smith et al., Mutat Res 173:273, 1986) and demonstrate induction of chromatin damage in the germ cells of male mice at doses lower than those previously used in studies involving single or multiple acute administration. (Supported by NTP NIEHS Contract # N01-ES-65141)

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ASSESSMENT OF THE BIOLOGICAL ACTIVITY OF MAINSTREAM OR ENVIRONMENTAL TOBACCO SMOKE (ETS) USING A CELLULAR SMOKE EXPOSURE TECHNIQUE. D. W. Bombick*, P. H. Ayres*, P. R. Nelson*, C. R. E. Coggins*, D. France*, C. Fulp*, C. Lee and D. J. Doolittle. R. J. Reynolds Tobacco Company, Winston-Salem, NC 27102.

The development of appropriate methods for exposing cell cultures to whole smoke are necessary for evaluating the biological activity of environmental tobacco smoke (ETS) in mammalian and bacterial cells. The cellular smoke exposure technique (CSET) uses a rocking apparatus that allows cells to oscillate between exposure to a known smoke concentration and culture medium maintained at 37°C. The neutral red assay in WB rat liver cells and an Ames assay were used to assess cytotoxicity and mutagenicity, respectively. Mainstream smoke generated from 1R4F reference cigarettes was used to characterize the CSET. WB cells were exposed for one or two hours to varying mainstream smoke concentrations (40 to 640 mg total particulate matter(TPM)/m³). The TA98 Salmonella bacteria were exposed for two hours to a mainstream smoke concentration of 320 mg TPM/m³. The cytotoxicity of 1R4F mainstream smoke to rat liver cells was concentration and time dependent with no observed effect levels for one and two hour exposures of approximately 160 and 40 mg TPM/m³, respectively. The TA98 Salmonella strain exhibited approximately a two-fold increase in the number of revertants/plate after exposure to 1R4F mainstream smoke and an S9 metabolic activation system. WB rat liver epithelial cells and the TA98 Salmonella bacterial strain were exposed to a relevant concentration of ETS (approximately 1.5 mg TPM/m³) for three hours. Using the neutral red cytotoxicity and Ames mutagenesis assays there were no differences observed in the ETS-exposed cells and their respective room air controls, indicating that ETS was biologically inactive as tested. The use of CSET permits determination of concentration X time relationships and threshold concentrations for the biological effects of mainstream, sidestream and environmental cigarette smoke without resorting to artificial smoke collection methods.

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SPATIAL DISTRIBUTION OF SPERM-DERIVED CHROMATIN IN ONE-CELL FERTILIZED EGGS. B. F. Brandriff, L. A. Gordon* and B. Trask*, Lawrence Livermore National Laboratory, Livermore, CA.

When a sperm enters an egg's cytoplasm at fertilization, the volume of its nucleus expands from a few cubic microns into several thousand cubic microns during the formation of the male pronucleus. During this transformation, which is carried out by biochemical factors stored in the egg cytoplasm during oogenesis, sperm-specific proteins are replaced by somatic histones, nucleosome structure is restored, and the genetically-inactive sperm DNA is reactivated. We tested the hypothesis that, in view of the large nuclear volume and the presence of a haploid, rather than diploid, chromosomal complement, the proximity of DNA sequences in male pronuclear chromatin might be very different from that in a small, diploid, somatic nucleus. For this purpose, we utilized an experimental system in which eggs from the golden hamster were fused with individual human or hamster sperm, and were followed in their development through the first cell cycle. This system allowed us to use DNA probes for hamster and human DNA sequences for which genomic distances in kilobase pairs (kbp) were known. Genomic distances could be compared to physical distances measured between the sites of the probes in pronuclei. The sites were detected by fluorescence *in situ* hybridization. We found that mean physical distances between signals in pronuclear chromatin were about three times those measured in fibroblasts. We also found a linear relationship between genomic and physical distances from 18 kbp up to at least 810 kbp. These data demonstrate that pronuclear chromatin is more loosely packaged than chromatin in somatic interphase nuclei. This unusual chromatin expansion may be one factor in explaining the preponderance of chromosome breakage events over chromosome rejoining events when sperm damage sustained before sperm-egg fusion is monitored at the first cleavage division. Work performed by the Lawrence Livermore National Laboratory under the auspices of the US Department of Energy, under contract W-7405-ENG-48.

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DIETARY INFLUENCES ON SPERMATOGENESIS. M.R. Brinkworth* and Diana Anderson, Genetic & Reproductive Toxicology Dept., BIBRA Toxicology International, Woodmansterne Road, Carshalton, Surrey, SM5 4DS, UK.

Currently there are no widely accepted [illegible] for studying the effects of [illegible] status on reproductive toxicology [illegible]-points. This paper describes two related [illegible] contrasting systems that were investigated [illegible] principally by using a sperm morphology [illegible]. Chronic protein deficiency [illegible] weeks) was examined in marmosets [illegible] subacute methionine- and choline-deficiency was investigated in F344 rats. The marmosets lost weight and were presumably

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